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Re-evaluation Note REV2016-02

Special Review Decision: Imazapyr

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Special Review Decision

Pursuant to subsection 17(2) of the *Pest Control Products Act*, Health Canada's Pest Management Regulatory Agency (PMRA) initiated a special review of all registered pest control products containing imazapyr, based on the 2001 Norwegian decision to prohibit all uses of imazapyr in Norway due to environmental concerns. The PMRA evaluated the aspects of concern that prompted the special review in accordance with the subsection 18(4) of the *Pest Control Products Act*. The proposed special review decision was published for consultation in the Re-evaluation Note REV2014-03, *Special Review of Imazapyr: Proposed Decision for Consultation* (Canada, 2014a) and it outlines the Agency's proposed decision and the reasons for it. Appendix I summarizes the comments received during the consultation period and provides the PMRA's response to these comments.

Comments received during the consultation process were taken into consideration in making this special review decision, and they did not result in changes to the proposed regulatory decision as described in REV2014-03. Therefore, the PMRA, under the authority of the *Pest Control Products Act*, is confirming the current registration of pest control products containing imazapyr in Canada. Additional advisory statements are required on the label to meet the current labelling standard (Appendix II).

Please refer to the Regulatory Directive DIR2014-01, *Approach to Special Reviews*, for details of the PMRA's special review approach.

Other Information

Any person may file a notice of objection[1] regarding this decision on imazapyr within 60 days from the date of publication of this special review decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of Health Canada's website, Request a Reconsideration of Decision, or contact the PMRA's Pest Management Information Service.

[1] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Comments and Responses

The PMRA received comments from stakeholders in response to Re-evaluation Note REV2014-03, *Special Review of Imazapyr: Proposed Decision for Consultation*. The PMRA consolidated and summarized the comments related to this special review and provides responses below.

1.0 Scope of the special review of imazapyr

1.1 Comment on the information considered by the PMRA for the special review

A special review conducted pursuant to subsection 17(2) of the *Pest Control Products Act* should give thorough consideration to the concerns leading to a prohibition on the use of the active ingredient in another country to assess whether the risk and value of the product are acceptable for continued registration in Canada. This should include obtaining and analyzing relevant data. It may also provide an opportunity to consider new information on emerging issues that may not have been available to or considered previously by the PMRA or the country with a prohibition in place.

PMRA Response

When a special review is initiated under subsection 17(2) (i.e. based on the prohibition of all uses of an active ingredient for health or environmental reasons in an OECD member country), the PMRA carries out an analysis of the OECD decision to identify the aspect(s) of concern related to the pest control products (i.e. the concern(s) that resulted in the prohibition of the active ingredient in the OECD country). For imazapyr, the aspect of concern that prompted the special review was identified as the potential for imazapyr to leach to groundwater. The aspect of concern is then evaluated as required under subsection 18(4) of the *Pest Control Products Act*.

Following the initiation of special review of imazapyr, the PMRA requested information from all provinces and other relevant federal government departments and agencies in accordance with subsection 18(2) of the *Pest Control Products Act*. The PMRA has considered available relevant scientific information, which includes information available from Norway related to the aspect of concern, recent available ground water monitoring information and information considered for the re-evaluation and registration of imazapyr. Information considered for special review, including that from Norway, was referenced in REV2014-03. Based on this information, the PMRA assessed imazapyr's fate in the environment, potential levels in groundwater using water modelling, as well as water monitoring information. In addition, the PMRA conducted a dietary risk assessment (considering the toxicity of imazapyr and potential exposure levels from the use of end use products in both food and groundwater) and determined that dietary exposure to imazapyr in drinking water (and food) is not of concern. On the basis of this scientific risk assessment, the PMRA concluded that, while no risk of concern was identified for pest control products containing imazapyr under the current conditions of use, additional advisory statements are required on the label to meet the current labelling standard (Appendix II).

1.2 Comment on pest control products under special review

The PMRA is focusing special reviews on the active ingredients and not on registered end-use products containing these active ingredients as required by the *Pest Control Products Act*. Although REV2014-03 states that the proposed special review decision is applicable to all registered products containing imazapyr, the proposed special review of imazapyr did not evaluate or summarize any evaluation of these registered products. An evaluation of a registered pest control product would assess the product itself, such as its value and conditions of use. There is nothing in the proposed special review document that suggests an evaluation of risks, value and specific use conditions was conducted for any registered products containing imazapyr.

In addition, two currently registered pest control products (Salute and Habitat) are not listed in Appendix I of REV2014-03. As they were registered after the publication of the proposed special review, presumably, these products were also not evaluated in the special review of imazapyr. To register new products containing imazapyr while conducting a special review to determine whether any products containing imazapyr should continue to be registered could reasonably be understood as an indication that the PMRA has pre-determined the outcome of this special review.

PMRA Response

Under the *Pest Control Products Act*, a special review of all registered pest control products containing the active ingredient in question is required. Therefore, as part of this special review, the PMRA considered all registered pest control products (technical, manufacturing concentrate and end-use products) containing imazapyr, and the special review decision is applicable to all registered products. Appendix I of REV20014-03 included the list of registered products containing imazapyr as of 6 May 2014. As noted in the comment, this list did not include two products: Salute B Herbicide (Registration Number 31504) and Habitat (Registration Number 30841) that were registered after 6 May 2014. However, the special review decision and the label amendments are applicable for all currently registered pest control products containing imazapyr. The PMRA considered the registration for these two products before making the final special review decisions. The registered use of Salute B (Registration Number 31504) is encompassed by the registered product ARES (Registration Number 30188, listed in Appendix I of REV2014-03), and, as such, the special review evaluation undertaken by PMRA is equally applicable to Salute B. Habitat (Registration Number 30841) was granted registration for emergency use for the control of invasive *Spartina* species outbreak in tidal areas along the coast of British Columbia only (i.e. the use is restricted to this region and is a time limited use). Based on this limited use pattern, potential risk to human health or the environment is not of concern.

When assessing the potential of a chemical to leach to groundwater, the PMRA considers the environmental chemistry and fate information from laboratory and field studies, ground monitoring information, as well as the existing risk-reduction measures included on all product labels related to the aspect of concern. While the laboratory studies in general are carried out with technical active ingredients, the field studies are conducted with end-use products containing the active ingredient under actual conditions of use in the field.

Additionally, the monitoring data gives an indication of the fate of the active ingredient when used as a formulated product under actual use scenarios. As part of this special review decision, the PMRA included additional advisory statements on the label to meet the current labelling standard (Appendix II).

Furthermore, it is important to reiterate that the scope of special reviews is limited to the aspect(s) of concern that prompted the special review, as per subsection 18(4) of the *Pest Control Products Act*. Value is not part of a special review initiated on the basis of subsection 17(2) of the *Pest Control Products Act*. It is the health or environmental concern(s) related to the pest control product that led to the ban in the OECD country that is the subject of a special review initiated on the basis of subsection 17(2).

1.3 Comment on water monitoring information

The proposed decision states that no Canadian groundwater monitoring data on imazapyr is available but does not indicate any efforts on the part of either the PMRA or the registrant to obtain such data. The special review is an opportunity for the PMRA to obtain Canadian data on imazapyr contamination and total pesticide loading in groundwater. Once obtained and analyzed, the results should be made public and considered in a revised proposed decision for consultation.

PMRA Response

As noted in Section 4.0 of REV2014-03, for the special review of imazapyr, the PMRA sought water monitoring information from Canadian and American monitoring sources. No Canadian water monitoring information on imazapyr was received upon request; however, the available American monitoring information was considered in the special review (REV2014-03, Section 5.0). The PMRA determined that exposure to pest control products containing imazapyr through drinking water is not of concern under the current conditions of use based on a scientifically based risk assessment. As noted in response 2.2, the aggregate exposure to imazapyr from food and drinking water, which is less than 0.1% of the acceptable daily intake (ADI) for all population subgroups, is well below the level of concern. Therefore, no additional water monitoring information is required at this time, as part of the special review for the currently registered uses.

2.0 Science evaluation

2.1 Comment on PMRA approach to drinking water assessment

Norway prohibited the use of imazapyr in 2001 due mainly to concerns for the contamination of groundwater caused by its persistence and high mobility in soil. Norwegian regulations state that no pesticide should contaminate drinking water in concentrations above 0.1 µg/L, and modelling suggests that imazapyr contamination in groundwater may exceed this threshold. The PMRA estimated concentrations of imazapyr in groundwater ranges from 2.0 to 36 µg a.i./L. This is 20 to 360-fold higher than Norway's threshold value. Likewise, monitoring in the States of Montana identified some concentrations 110 times greater than Norway's value.

REV2014-03 explains that the PMRA drinking water risk assessment takes into account toxicity, as well as estimated concentrations in drinking water, and that higher concentrations of imazapyr are considered acceptable because of its low toxicity at these concentrations.

This approach ignores the cumulative and synergistic risks of multiple substances contaminating drinking water, combined with other pathways of exposure. The PMRA should give thorough consideration to the more precautionary rationale leading to a prohibition of the use of the active ingredient in Canada.

PMRA Response

The PMRA considers cumulative health effects of pest control products when a common mechanism of toxicity is identified with other pest control products. Health Canada's Science Policy Notice SPN2001-01, *Guidance for Identifying Pesticides that have a Common Mechanism of Toxicity for Human Health Risk Assessment*, describes the steps for identifying mechanisms of toxicity of pesticides that cause a common toxic effect, the types of data needed and their sources, how these data are to be used in reaching conclusions regarding commonality of mechanisms of toxicity, and the criteria Health Canada applies for categorizing pesticides for the purpose of cumulative risk assessments. For imazapyr, no common mechanism of toxicity has been identified with other pest control products. Therefore, no cumulative risk assessment was required for imazapyr.

The Norwegian Drinking Water Regulations (Regulation Number 1372) set quality standards for drinking water in Norway including a threshold of 0.1 µg/L for any individual pesticide in water intended for human consumption. The 0.1 µg/L threshold is a legislated rather than risk-based value that applies to all pesticides regardless of their toxicity to humans. The PMRA follows a risk-based scientific approach in determining the risk to human health from pesticides in drinking water. As noted in the comment, this approach takes into consideration both the estimated level in drinking water sources and the toxicity of the pesticide. Based on the exposure and risk assessment, the PMRA concludes that there are no risks of concern from groundwater under the current conditions of use.

2.2 Comment on the PMRA's drinking water risk assessment

It is unclear why the PMRA is using two different maximum application rates for assessing groundwater contamination concentrations versus drinking water concentrations. For the former, the maximum food crop application rate is used (9 g a.i./ha). For the latter, double the much higher maximum overall rate is used (1.69 kg a.i./ha). While we can appreciate the need to be conservative on the drinking water assessment, we do not understand why the PMRA would limit the environmental assessment to the much lower maximum food crop application rate.

PMRA Response

The aspect of concern identified for the special review of imazapyr was the potential for leaching to groundwater.

For the special review, the PMRA considered the estimated environmental concentration of imazapyr in ground water based on modelling, and, water monitoring information. As the use pattern of imazapyr in the United States encompasses the use pattern in Canada, PMRA considered the estimated drinking water concentration at the highest registered American application rate of 1.69 kg a.e./ha, (79 µg/L for surface water (FIRST model) and 36 µg/L for groundwater using SCI-GROW model). Based on this, the aggregate exposure (food and water) was 0.1% of the ADI for all population subgroups, which is not of concern.

2.3 Comment on PMRA risk management

The proposed decision suggests that the potential for imazapyr contamination in groundwater in Canada is minimized by advisory environmental hazard statements on the label of end-use products. These measures are significantly less protective than the prohibition of use implemented in Norway to address the same issue. At a minimum, the PMRA should assess enforcement/compliance with labelled risk reduction measures and the effectiveness of precautionary statements in reducing contamination in groundwater.

PMRA Response

The PMRA determined that exposure to imazapyr through drinking water is not of concern under the current conditions of use based on a scientifically-based risk assessment. As noted in REV2014-03, the aggregate exposure to imazapyr from food and drinking water is well below the level of concern for all population subgroups. The precautionary label statements (including the required label amendment specified in Appendix II) along with other mitigation measures (e.g. spray drift buffer zones) included on the product labels are intended to further reduce the potential risk to humans and the environment. In addition, the PMRA takes a risk-based approach for the compliance and enforcement program, routinely conducts active prevention and monitoring programs across the regulated community, and, follows up on situations of reported or suspected pesticide misuse. This is done in partnership with our federal and provincial colleagues.

2.4 Comment on non-target terrestrial plants and aquatic vascular plants

According to the USEPA 2006 Reregistration Eligibility Decision for imazapyr "…there are ecological risks of concern associated with the use of imazapyr for non-target terrestrial plants and aquatic vascular plants, and potential risks to federally listed threatened and endangered species ("listed species") which include aquatic vascular plants, terrestrial and semi-aquatic monocots and dicots that cannot be precluded at this time. Imazapyr use at the labeled rates on non-crop areas when applied as a spray or as a granular to forestry areas present risks to non-target plants located adjacent to treated areas."

In light of concerns leading to a ban in Norway (notably imazapyr's persistence and mobility in soil), the PMRA should assess the effectiveness of labelled risk reduction measures in protecting threatened and endangered species in Canada in particular.

PMRA Response

In accordance with subsection 19(4) of the *Pest Control Products Act*, the PMRA is required to assess the aspect of concern identified in the OECD member country decision. The Norwegian decision to prohibit all uses was not based on the risk to non-target organisms, but rather on the potential to leach to groundwater. As part of the special review, the PMRA assessed the potential leaching of imazapyr to groundwater, as well as the risk from exposure to potential residues in drinking water, and identified no health concern.

As a part of PMRA's re-evaluation and registration decisions, the PMRA assessed potential risk to non-target organisms. As a result, precautionary label statements along with other mitigation measures (e.g. spray drift buffer zones) intended to further reduce the potential risk to the environment are currently included on the product labels. More generally, there are post-market mechanisms in place, such as active prevention and monitoring compliance programs, as well as mandatory incident reporting, that allow the PMRA to continue to monitor the safety of these products, including potential exposures to non-target organisms.

2.5 Comment on chronic exposure assessment

The PMRA has assessed that chronic exposure is less than 0.1% of the acceptable daily maximum intake of 2.53 mg/kg bw/day for all population subgroups, below the level of concern. However, it is impossible to ascertain how all population subgroups were accounted for because the PMRA does not disclose the calculations on which this is based on, other than to say it was a 24-month rat combined chronic/carcinogenicity study. It is therefore very difficult to assess the safety and acceptability of the NOAEL. This has implications for the reasonableness of the PMRA's decision to not apply the 10-fold *Pest Control Products Act* factor under section 19(2)(b)(iii).

PMRA Response

As indicated in REV2014-03, risk from aggregate exposure to imazapyr from food and drinking water was assessed based on an ADI of 2.53 mg/kg bw/day. The 24-month rat combined chronic/carcinogenicity study was selected for risk assessment with a NOAEL of 253 mg/kg bw/day. This was the lowest NOAEL in the database and was relevant for the establishment of the ADI. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the *Pest Control Products Act* Hazard Consideration response (response to comment 2.8), the *Pest Control Products Act* factor was reduced from 10-fold to 1-fold. The composite assessment factor (CAF) is 100. The selection of the ADI was described in Proposed Registration Decision PRD2011-12, *Imazapyr* (Canada, 2011).

Based on the highest estimated drinking water concentrations, the aggregate exposure (food and water) was 0.1% of the ADI for all population subgroups, including the highest exposed population subgroup, infants < 1 year old. Therefore, there is no health risk of concern.

As indicated in REV2014-03, the drinking water risk assessment was based on an ADI. An acute reference dose (ARfD) was not established as there were no acute endpoints of concern identified in the imazapyr database. A cancer endpoint was also not identified for imazapyr.

The chronic dietary exposure was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI to determine risk. Chronic dietary risk is not of concern, when the expected intake of residues is less than the ADI.

For food uses, dietary exposure from food and drinking water was conducted using the estimated groundwater concentration specific to imazapyr food-crop uses in Canada (i.e. 2.0 µg a.i./L, calculated using the LEACHM model and an application rate of 9 g a.i./ha) and assumed 100% crop treated. Results indicated that imazapyr exposure by this route was negligible for all population subgroups. Thus, aggregate exposure from food and water is not of concern. All population subgroups were considered, including the highest exposed population, children 1-2 years old.

For non-food uses, the PMRA considered the highest drinking water concentrations estimated from surface water modelling, 79 µg/L. [Note: 36 µg/L for groundwater (SCI-GROW model)] Aggregate exposure from food and water, assuming 100% crop treated and using default processing factors, was less than 0.1% of the ADI for all population subgroups, including the highest exposed population subgroup, infants < 1 year old. Therefore, there is no health risk of concern.

2.6 Comment on other routes of exposure

There is no consideration of other sources of aggregate exposures to pest control products containing imazapyr, such as dermal exposure and inhalation, both of which are typical exposures for persons applying imazapyr products. As required by law, the special review must evaluate available information on aggregate exposure including dietary exposure and exposure from drinking water.

PMRA Response

In accordance with subsection 16(4) of the *Pest Control Products Act*, the PMRA assessed the aspect of concern. The aspect of concern identified for the special review of imazapyr was the potential for leaching to groundwater. In addition to assessing the potential for imazapyr to reach groundwater, the PMRA has conducted a scientifically-based drinking water risk assessment to determine whether exposure to imazapyr through Canadian groundwater presents an unacceptable risk to Canadians. Since the Canadian population can also be exposed to imazapyr from other sources (i.e. food), aggregate exposure to imazapyr was also considered as part of the special review.

As described in REV2016-03, aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation). Science Policy Notice SPN2003-04, *General Principles for Performing Aggregate Exposure and Risk Assessments*, describes the overall framework and the general principles followed by the PMRA when performing an aggregate exposure and risk assessment.

Residential and other non-occupational exposure to imazapyr (including use around home and suburbs) is not expected to occur under the currently registered use pattern. Therefore, aggregate exposure to imazapyr is limited to food and drinking water only and there is no risk of concern from the aggregate exposure (response to comment 2.7).

2.7 Comment on cumulative effects of the pest control products

Subsection 19(2)(b)(ii) of the *Pest Control Products Act* requires the PMRA to evaluate the "cumulative effects of the pest control product and other pest control products that have a common mechanism of toxicity". The proposed special review decision for imazapyr declines to assess any cumulative effects.

The PMRA does not assess the cumulative effects of the many registered pest control products listed in Appendix I that all contain imazapyr. Clearly these eight products, including Sahara B Herbicide, have common mechanisms of toxicity. The PMRA does not assess the cumulative effects of the three of these eight pest control products that also contain the second active ingredient of imazamox. If products containing imazamox have a common mechanism of toxicity, cumulative effects should be assessed. The PMRA does not rule out the likelihood that these eight pest control products have common mechanisms of toxicity with other pest control products in Canada. Rather, the PMRA simply concludes that no common mechanism of toxicity has been identified for imazapyr and other active ingredients. The PMRA's failure to identify common mechanisms of toxicity does not mean these do not exist, again, to rely on a lack of full scientific certainty as a justification for not assessing cumulative effects would be inconsistent with the precautionary principle. Importantly, in deeming there to be no common mechanism of toxicity that would require a cumulative effect assessment, the mechanism of toxicity that the PMRA considered is not disclosed. The PMRA must evaluate the cumulative effects of products containing imazapyr in combination with other pest control products with a common mechanism of toxicity.

PMRA Response

As noted in REV2016-03, the PMRA considers cumulative health effects of pest control products when a common mechanism of toxicity is identified with other pest control products. Health Canada's Science Policy Notice SPN2001-01, *Guidance for Identifying Pesticides that have a Common Mechanism of Toxicity for Human Health Risk Assessment*, describes the steps for identifying mechanisms of toxicity of pesticides that cause a common toxic effect, the types of data needed and their sources, how these data are to be used in reaching conclusions regarding commonality of mechanisms of toxicity, and the criteria Health Canada applies for categorizing pesticides for the purpose of cumulative assessment. A common mechanism of toxicity has not been identified for imazapyr and other pest control products, nor is this active ingredient

considered to produce a metabolite common to other active ingredients. Therefore, a cumulative assessment is not required. Similarly, a common mechanism of toxicity has not been identified for insomnox and other pest control products, nor is this active ingredient considered to produce a metabolite common to other active ingredients. Therefore, a cumulative assessment is also not required for insomnox.

5.6 Comments on *Pest Control Products Act* factor

Under subsection 19(2)(b)(iii) of the *Pest Control Products Act*, in respect of a threshold effect, the PMRA is obliged to apply a margin of safety that is ten times greater than the margin of safety that would otherwise apply under subsection 19(2)(b)(ii) if the pest control product is used in or around homes or schools. The proposed special review decision advises that the PMRA is not applying this higher margin of safety – that is, the "10-fold *Pest Control Products Act* factor" – to insomnox, or presumably to any pest control products containing insomnox.

Further, the PMRA decided to reduce the 10-fold *Pest Control Products Act* factor to 1. However, it is unclear whether this decision is justified or precautionary. The PMRA does not conclude that none of the many pest control products containing insomnox are not used in or around homes or schools. Furthermore, it appears that the PMRA's proposed decision not to use the 10-fold *Pest Control Products Act* factor in this special review may be inconsistent with the PMRA's published policy documents. According to the PMRA's Uncertainty Factor Guideline (dir2018-01), the PMRA "interprets the new *Pest Control Products Act* provisions as requiring a presumptive application of the 10-fold factor for the protection of infants and children. In other words, the onus is on the PMRA to provide a reliable scientific rationale in those cases where the 10-fold *Pest Control Products Act* factor is reduced". The PMRA has not provided any such reliable scientific rationale here, but merely stated that it assessed the toxicity database for children and infants to be complete and that there is "no indication of increased susceptibility to fetuses or offspring compared to parental animals in reproductive and developmental studies". Thus the PMRA appears to rely on a lack of data to assume safety, which is inconsistent with a precautionary approach. Furthermore, the PMRA does not address any data regarding exposure of infants and children, as is required under subsection 19(2)(b)(iii). Nor does the PMRA disclose which studies it relies on, making it impossible to assess if the rationale is reliable. Finally, the human health risk assessment of insomnox conducted for Washington State provides contrary evidence, namely the existence of possible endocrine effects which could create greater susceptibility to fetuses.

To be clear, the application of the 10-fold *Pest Control Products Act* factor may or may not be appropriate here, and may or may not change the PMRA's assessment of human health risks of pest control products containing insomnox. However, if the PMRA continues to conclude that it is not appropriate to apply the 10-fold *Pest Control Products Act* factor, a more transparent rationale is required, including an identification of the reliable scientific data relied upon with respect to both toxicity to and exposure of infants and children.

PMRA Response

As indicated in REV2014-03, for assessing risks from potential exposure, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. In accordance with the Science Policy Note, SPN2008-01, *The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment*, a different factor may, however, be determined to be appropriate on the basis of reliable scientific data.

The PMRA evaluated the toxicity database for imazapyr (Canada, 2011), and found that the database contains the full complement of required studies including developmental studies in rats and rabbits, and a reproductive toxicity study in rats. These studies indicated no increased susceptibility of fetuses or offspring compared to parental animals. There were also no developmental effects observed in the rat and rabbit developmental study. On the basis of no effects on fetuses and offspring, the *Pest Control Products Act* factor was reduced from 10-fold to 1-fold for imazapyr. The developmental and reproductive toxicity studies considered for establishing the *Pest Control Products Act* Factor for imazapyr are listed in Appendix I of Proposed Registration Decision PRD2011-12, *Imazapyr*.

The PMRA considered information submitted as part of the comments provided (*Human Health and Ecological Effects Risk Assessment, Imazapyr Risk Assessment, Washington State*). The overall assessment for human health concluded in this report as "Although there are some uncertainties associated with the risk assessment for human exposure to imazapyr, the highest hazard quotients with imazapyr exposures are substantially below levels of concern, indicating that human exposure to imazapyr poses little risk." The hazard identification section of the report (Section 3.2.1) states: "Multi-generation reproductive and developmental studies for imazapyr have demonstrated no adverse effects on reproductive capacity or normal development." The risk characterization section for sensitive subgroups (Section 3.5.4) states: "There is no information to suggest that specific groups or individuals may be especially sensitive to imazapyr. As indicated in Section 3.2, the mechanism of action for imazapyr is not well understood. It does not appear to specifically affect the nervous system (Section 3.2.8) or the immune system (Section 3.2.7) but there is suggestive evidence that it may affect endocrine function (Section 3.1.8).

Given the very low hazard quotients for imazapyr, there appears to be no basis for concern that certain groups are more sensitive to imazapyr or at greater risk due to imazapyr exposure. EPA (1997, 2003) has indicated that infants and children are not likely to be more sensitive to imazapyr than adults."

Based on the available information the PMRA concludes that a reconsideration of the reduction of the *Pest Control Products Act* factor to 1-fold for imazapyr is not warranted.

3.0 Special review process

3.1 Comment on Comment on initiating special reviews

The PMRA should develop a systematic approach to initiate a special review when a member country of the OECD prohibits all uses of an active ingredient for health or environmental reasons. It was noted that Norway's ban on imazapyr took effect in January 2001, but the PMRA did not initiate the legally required special review until December 2013.

PMRA Response

The PMRA continues to monitor the regulatory status in OECD member countries of products containing active ingredients registered in Canada. The PMRA seeks information through participation in international working group meetings such as the OECD and the Rotterdam Convention, as well as from the publicly available databases.

Appendix II – Label Amendments for Imazapyr

The label of imazapyr end-use products must be amended to include the following statements.

Add to ENVIRONMENTAL HAZARDS:

"This product demonstrates the properties and characteristics associated with chemicals detected in groundwater. The use of [product name] in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination."

References

Published Information

PMRA Number	Reference
2098183	Canada, 2011. Proposed Registration Decision PRD2011-12, Imazapyr.
2451837	Canada, 2014a. Re-evaluation Note REV2014-03, Special Review of Imazapyr: Proposed Decision for Consultation.
	Canada, 2014b. Science Policy Note SPN 2014-01, General Exposure Factor Inputs for Dietary, Occupational, and Residential Exposure Assessments.